



Response to Office Action dated November 30, 2006:

1. EXAMINER'S ALLEGATION THAT PATENT IS VAGUE AND INDEFINITE.

Claims 1-14 were rejected under the allegation that they are indefinite under 35 USC 112. The examiner has stated that Claim 1 and its dependents are "drawn to a culture medium", but are "vague and indefinite" for failing to particularly point out and distinctly claim the subject matter which was regarded as the invention. The examiner states that this is because the language "are configured" contained in line 6 "implies that a step is taken to configure the inhibitors in a particular way which is not recited in the claim". The constituent contents of the medium and the configuration of those contents are identified and described in detail in the patent application. The phrase "are configured" was used in the patent application document to refer to the configuration described within that document. This phrase was used only in its common sense application to the configuration described within the patent application. Any attempt to read into the phrase an inference that some additional configuration beyond that described in the patent application was unnecessary to a common sense reading of the language and was erroneous.

2. EXAMINER'S ALLEGATION THAT THE CLAIMED MEDIUM WAS ANTICIPATED BY HEIFETS.

The second basis for rejecting the application was based on 35 U.S.C. 102 (b) as anticipated by Heifets. A summary of the examiner's argument is that the components in the Heifets medium are not structurally different from those contained in the current application and that even if the Heifets medium does not teach the same functions as those claimed in the current medium, since the components are the same, the functions and uses of those components must have been present in Heifets medium and therefore Heifets anticipated the claimed medium. The examiner is mistaken. The components are not the same. They are different because the intended functions of the two media require structural differences as set out below.

The Heifets medium is formulated for one purpose only. It is a factory for the efficient production of mycobacteria. Its intended function determines its contents. The only purpose of the contents of Heifets medium is to facilitate the growth and production of mycobacteria. The mycobacteria grown in Heifets' medium can be harvested and utilized in various ways. However, the medium of Heifets has no intended use beyond the production of mycobacteria.

The medium described by the current claims is utterly different. It is not a mycobacteria factory. It is a rapid diagnostic medium. It is structurally different because it was conceived of as a rapid diagnostic medium rather than as a mycobacteria factory. The examiner has acknowledged that the Heifets medium did not teach the claimed functions of each of the components in the medium but she argued that the components were the same and based on that assumption, the examiner argued that even if there were unappreciated properties in the prior art's composition, those functions were inherently present and thus the claimed medium is not structurally different.

The examiner's argument is factually incorrect in stating that the components in Heifets' medium are the same as those in the claimed medium. The examiner is also incorrect in stating that one familiar with the art could utilize the components of Heifets' medium to perform the same functions as those in the claimed medium. One familiar with and even expert in the art could utilize every conceivable property of the components in the Heifets medium, either previously or currently appreciated, and she would never change the Heifets medium from a mycobacteria factory into a rapid diagnostic medium (a medium which indicates mycobacterial growth early).

The claimed medium is structurally different because it must contain different components to allow for pH change and to allow detection of that change. Allowing pH fluctuation is the opposite of the goal of any other mycobacteria growth medium including Heifets medium. It is by permitting pH change and then rapidly detecting the results of that change that the claimed medium can act as a rapid diagnostic medium. The claimed medium contains a pH indicator such as phenol red which the Heifets medium

does not. The examiner states at page 6 of the Office Action that the Heifets medium contains phenol red. It does not. Heifets refers to phenol red, but not in the composition of the Heifets medium. The Heifets application contains, in addition to the claims related to the constitution of Heifets medium, a description of a process that may be used in preparation of samples that are intended to be inoculated to the Heifets medium. The Heifets medium does not patent sample preparation. However, Heifets medium claim a medium that maintains a pH in a carefully contained range between 6.0 and about 6.25 (see Heifets claim 1). In maximizing mycobacterial growth, it is important that the pH level be stabilized in this narrow range. Therefore, a description of sample preparation is provided that will stabilize the pH of samples that can later be added to the Heifets medium so that those samples will not disrupt the pH range that the Heifets medium must maintain according to its claims. Again, the process of sample preparation takes place outside of the Heifets medium and is not part of the composition of the Heifets medium.

Heifets begins his description of sample preparation at 0189 in his application. He then identifies the addition of phenol red as part of the phosphate buffer solution at 0206. The phenol red, along with other elements of the supernatant solution are centrifuged (0218) to separate them from the bacteria that will form the inoculum and at 0219 the supernatant fluid containing the phenol red is decanted (disposed of) having performed its function of measuring the pH. Only the bacteria remain to be inoculated to Heifets medium. Thus, the phenol red is not a part of the Heifets medium and is never added to the Heifets medium.

As indicated above, a pH indicator is essential to devising a medium that can react to the changes in pH level in order to induce the spectroscopic changes that permit the diagnostic properties employed by the claim. Moreover, a pH indicator is only of value where the pH level will be allowed to fluctuate, rather than being tightly controlled which is the case in Heifets medium.

The examiner has stated that the absence of phenol red or a color dye indicator in Heifets' medium is not persuasive because Heifets' medium contains malachite green, which the

examiner states is a color dye pH indicator. The examiner is mistaken. Malachite green is not a color indicator but a bacteria inhibitor. It is generally used to eliminate contaminant bacteria other than mycobacteria. The name of this reagent includes the word "green" because this reagent is actually green but malachite green is never used as a color indicator. The Heifets medium contains a very small quantity of malachite green for the purpose of inhibiting the growth of organisms other than mycobacteria. Heifets' medium does not use malachite green as a color pH indicator. More importantly, malachite green cannot be used as a pH indicator or color dye indicator for the purpose of rapid indication of growth.

When mycobacteria grow in culture they produce acid substances which lower the pH of the medium. Heifets' medium contains phosphate salts which work as buffers to stabilize the pH of the medium. Because of that the pH of the Heifets' medium does not change markedly during mycobacterial growth. In the claimed medium, phosphate salts are not present which leads to a rapid pH change during mycobacterial growth. The pH change is used as an indicator of rapid growth by the claimed medium, which is detected by a color dye pH indicator such as phenol red. This idea, i.e., to detect the differential growth of mycobacteria is an original idea and has never before been stated or published. This idea comes directly from our original and internal research and development efforts and is the basis of our claims. When all the other known media and processes try to stabilize the pH for the growth of mycobacteria, the claimed medium is especially composed to allow pH fluctuation and detection of pH change.

For the reasons set forth above, the examiner is factually incorrect in stating that the components of Heifets' medium are the same as those in the claimed medium. They are structurally different as well as functionally different. Furthermore, no use of the components in the Heifets medium, whether arranged according to their intended use as a mycobacteria factory or in any other arrangement will allow the Heifets medium to function as a rapid diagnostic medium. Thus, no "functions or unknown properties" in components of the Heifets medium are "inherently present" in that medium that would

allow it to act as a rapid diagnostic medium. The claimed medium is structurally different and was not anticipated by the Heifets medium.

3. EXAMINER'S ALLEGATION THAT THE CLAIMED MEDIUM IS ANTICIPATED BY MIYAMOTO.

Claims 1 - 3 and 7 - 8 were rejected by the examiner under 35 U.S.C. 102(b) as being anticipated by Miyamoto et al. (US 6197574 B1). The examiner made essentially the same argument as that given for rejection of the claims as anticipated by Heifets. She alleged that the components are the same and the functions of those components are inherently present in the medium of Miyamoto. The examiner is incorrect in this case for the same reasons set forth above regarding the Heifets medium. Indeed, the media are even more different since the Miyamoto medium is not even intended to grow mycobacteria.

The most essential differences between the claimed medium and that of both Heifets and Miyamoto are stated above and all differences described between the claimed medium and Heifets' medium, apply equally to Miyamoto. It should be noted that the Miyamoto medium is a factory for producing bacteria other than mycobacteria. Nevertheless, like Heifets' medium, the Miyamoto medium is designed to produce bacteria and that is all it is designed to do and that is all its components are capable of doing. The Miyamoto medium lacks the essential components that would allow it to function as a rapid diagnostic medium for mycobacteria for all the same reasons stated above.

For completeness, it should be stated that the difference between the claimed medium and Miyamoto's medium based on the absence of albumin, an essential component in any mycobacteria medium, was improperly rejected by the examiner. Most of the widely used mycobacterial culture media, like Löwenstein Jensen, Ogawa, Coletsos contain egg (as albumin source) or media like Middlebrook contains bovine serum albumin. Albumin is needed to bind toxic substances produced in the medium by mycobacterial growth. The examiner stated that the absence of albumin in the Miyamoto medium was not a

persuasive difference because the claimed medium did not require albumin either. However, the claimed medium specifically notes the use of eggs (see claim number 5) which is a primary source for albumin.

4. EXAMINER'S 2nd ALLEGATION THAT THE CLAIMED MEDIUM WAS ANTICIPATED BY HEIFETS'.

The examiner's final argument again referred to Heifets' medium for rejection of claims 14-5 and 11 (I expect this is a typo and should read claims 4-5 and 11) but this time based the rejection on 35 USC 103(a). The examiner argued that even though the claimed medium uses antimicrobials and an egg based solution while the Heifets medium does not, this was not a persuasive difference because, according to the examiner, at the time of the invention, egg based gelling solutions were standard alternatives to agar and because, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Heifets to include known antimicrobials in the culture medium with a "reasonable expectation for successfully obtaining the effective medium of Heifets". I believe the examiner intended to state that the functions of the claimed medium would then be obtained by the Heifets medium.

The above argument is bootstrapped onto the same error as noted earlier in response to the examiner's first argument that Heifets medium anticipated the claimed medium. The examiner again assumed that the components of Heifets' medium are the same as those contained in the claimed medium. The assumption is not correct so adding egg based solutions or antimicrobials to the Heifets medium would never allow Heifets medium to function as a rapid mycobacterial diagnostic medium.

5. THE EXAMINER HAS ARGUED THAT THOSE OF ORDINARY SKILL IN THE ART COULD HAVE ACCOMPLISH THE CLAIMED MEDIUM BASED ON THE EXISTING ART OF HEIFETS' MEDIUM AND MIYAMOTO'S MEDIUM. THOSE WITH EXPERT SKILL IN THE ART RESPECTFULLY DISAGREE.

I have attached a statement from the Johns Hopkins Center for Global Health. As you can see, the Center was preparing to study the claimed medium, noting that it is a novel (emphasis added) solid culture medium for detection of M. tuberculosis. In the event you would like to see the original web page containing the attached document, it is found at: http://commprojects.jhsph.edu/globalhealth/GlobalProjectDetail.cfm?project_id=6812&country_code=SF.

In addition, I am attaching a copy of the press release from the Foundation for Innovative New Diagnostics (FIND), a nonprofit organization whose purpose, as noted in their mission statement and statement of objective is as follows:

FIND is a leading non-profit organization dedicated solely to the development of rapid, accurate and affordable diagnostic tests for poverty-related diseases in the developing world. Its mission is driven by the conviction that good health is central to winning the war against poverty and that correct diagnosis is a crucial first step towards establishing health and thus efficient use of resources. To develop, in partnership with academia, public and private research institutes and industry, new (emphasis added) diagnostic approaches that have been proven in principle and to transform them into effective products for identifying poverty-related diseases.

FIND stated in the attached statement that they were adding the claimed medium to their development portfolio because it is a novel tuberculosis colorimetric medium.

Please refer to the FIND team résumés at the following web link where you will see that the entire team is composed of high level experts in the field of microbiology and tuberculosis research. <http://www.finddiagnostics.org/about/team/index.shtml>

The point of the attached references is that the experts, much less those with ordinary skill in the art, have not previously succeeded in taking the existing art as represented by the mediums of Heifets and Miyamoto and developed the much needed diagnostic medium now presented in the claimed medium. Had the claimed medium been obvious

they would have done so. For the reasons set forth above, it was not possible for them to do so. In fact, the experts in the field recognize the claimed medium as new and novel.

Conclusion

For the reasons set forth above, it is clear that the claimed medium is a novel invention that is structurally different from the referenced prior art and no method utilizing the components of the prior art would permit them to accomplish the novel functions of the claimed medium. For the reasons set forth above, I respectfully request that the prior Office Actions rejecting the claimed medium be rescinded and that the patent be allowed.

Respectfully Submitted,

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Director of Regulatory and Legal Affairs
SALUBRIS, Inc.

Resubmitted with Req. to Revive On:
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